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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/963,790	09/27/2001	Mike Farwick	32301WD230	9133

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/963,790	FARWICK ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,9,12,34,35,37,38,40,42-48 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5,9,12,34,35,37,40,42,53 and 54* is/are allowed.

6)☒ Claim(s) *43,51 and 52* is/are rejected.

7)☒ Claim(s) *44,46 and 48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5-08

DETAILED ACTION

Status of the Application

[1] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[2] The finality of the rejection of the last Office action is withdrawn. According to MPEP 706.07(d), "if ... the primary examiner finds the final rejection to have been premature, he or she should withdraw the finality of the rejection." In view of the new rejection(s) presented below, the instant Office action is a non-final Office action.

[3] Claims 5, 9, 12, 34-35, 37-38, 40, 42-48, and 51-54 are pending in the application.

[4] Applicants' amendment to the claims, filed 7/27/2005, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[5] Applicants' arguments filed 7/27/2005 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[6] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objection

[7] Claim 38 is objected for the use of the improper alternative expression "any of the claims 5, 9, 34 or 37." It is suggested that the expression be replaced with, for example, "any one of claims 5, 9, 34 or 37."

[8] Claims 45 and 47 are objected to under 37 CFR 1.75 as being substantial duplicates of claim 42. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). While it is acknowledged that claims 45 and 47 recite different intended uses for the claimed nucleic acids, these intended uses do not further limit the nucleic acid. Applicants are advised that, should applicants amend claims 45 and 47 to recite "at least 40 consecutive nucleotides" to overcome the instant objection, claim 47 would then appear to be identical in scope to claim 45.

Claim Rejections - 35 USC § 112, First Paragraph

[9] Claims 43 and 51-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention.

Initially, it is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." It is noted that,

while claim 43 (claim(s) 51-52 dependent therefrom) recites the closed transitional phrase "consists of" referring to the isolated polynucleotide of the vector, the vector is "comprising" the polynucleotide. Regarding the transitional phrase "comprising," MPEP 2111.03 states, comprising "is inclusive or open-ended and does not exclude additional, unrecited elements." As such, the vector may include additional encoding sequence at the 5' and or 3' ends of the recited polynucleotide. Accordingly, claim 43 is drawn to a genus of vectors comprising a polynucleotide as few as 30 consecutive nucleotides of SEQ ID NO:1 or the complement thereof.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the claimed genus of vectors, *i.e.*, a vector comprising a polynucleotide encoding SEQ ID NO:2 or the complete complement of a polynucleotide encoding SEQ ID NO:2. The specification

fails to describe any additional representative species of the claimed genus of nucleic acids. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the recited genus of vectors encompasses species that are widely variant in both structure and function, including (but not limited to) nucleic acids encoding polypeptides that have function other than the DNA/RNA helicase activity of SEQ ID NO:2, including non-functional polypeptides. As such, the disclosure of the single representative species of vectors is insufficient to be representative of the attributes and features of all species encompassed by the claimed invention.

Given the lack of description of a representative number of vectors, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[10] Claims 43 and 51-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vector comprising a polynucleotide encoding SEQ ID NO:2 or the complete complement of a polynucleotide encoding SEQ ID NO:2, does not reasonably provide enablement for all vectors as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: As noted above, claim 43 (claim(s) 51-52 dependent therefrom) is so broad as to encompass vectors comprising a polynucleotide as few as 30 consecutive nucleotides of SEQ ID NO:1 or the complement thereof, with any additional sequence at the 5' and/or 3' end(s) of the polynucleotide. The enablement provided by the specification is not commensurate in scope with the claims with regard

to broad scope of vectors as encompassed by the claims. In this case, the specification is enabling only for a vector comprising a nucleic acid encoding SEQ ID NO:2 or the complete complement of a polynucleotide encoding SEQ ID NO:2.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: The nucleotide sequence of an encoding nucleic acid determines the encoded protein's structural and functional properties. Predictability of which changes can be tolerated in an encoded protein's amino acid sequence and obtain the desired activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (*i.e.*, expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, *e.g.,* multiple substitutions. At the time of the invention, methods for isolating or generating variants and mutants of a given nucleic acid were known in the art. However, neither the specification nor the state of the art at the time of the invention provide the necessary guidance for altering the nucleotide sequence of SEQ ID NO:1, *i.e.,* taking as few as 30 nucleotides of SEQ ID NO:1 or the complement thereof and adding back sequence to the 5' and/or 3' ends, with an expectation of obtaining an encoded polypeptide having the desired

activity/utility. At the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). The teachings of Branden et al. are exemplified by the reference of Witkowski et al. (*Biochemistry* 38:11643-11650), which teaches that only a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see *e.g.*, Table 1, page 11647).

The amount of direction provided by the inventor and The existence of working examples: The specification discloses only a single working example of the claimed vector, *i.e.*, a vector comprising a nucleic acid encoding SEQ ID NO:2 or the complete complement of a polynucleotide encoding SEQ ID NO:2. The specification fails to disclose any specific guidance for altering the nucleotide sequence of SEQ ID NO:1 with an expectation that the resulting variants of SEQ ID NO:1 or the complement thereof within the claimed vector will encode a polypeptide that maintains the desired activity/utility.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating or generating variants of an encoding nucleic acid were known in the art at the time of the invention, it was not routine in the art to screen – by a trial and error process – for all nucleic acids having a substantial number of modifications as encompassed by the claims for those nucleic acids that encode a polypeptide having the desired activity/utility.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

[11] Status of the claims:

- Claims 5, 9, 12, 34-35, 37-38, 40, 42-48, and 51-54 are pending.

- Claims 38, 45, and 47 are objected to but would otherwise appear to be allowable.
- Claims 43 and 51-52 are rejected.
- Claims 44, 46, 48 are objected to as being dependent upon an objected/rejected base claim, but would otherwise appear to be allowable.
- Claims 5, 9, 12, 34-35, 37, 40, 42, and 53-54 appear to be in a condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs and alternate Fri, 7:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656